



SEQUENCE LISTING

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Renshaw, Mark  
Orencia, Cecilia

<120> RATIONALLY DESIGNED ANTIBODIES

<130> 1087-2 CIP III

<140> US 10/737,290  
<141> 2003-12-15

<150> US 10/452,590  
<151> 2003-06-02

<150> US 10/307,724  
<151> 2002-12-02

<150> US 10/006,593  
<151> 2001-12-05

<150> US 60/251,448  
<151> 2000-12-05

<150> US 60/288,889  
<151> 2001-05-04

<150> US 60/294,068  
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<170> PatentIn version 3.2

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Gly Gly

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Gly Gly

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Pro Val

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Pro Ile

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 ctgcgcgaac aggtggcaca gctgaaacag aaagttatga accatggcgg ttgtgctagt 180  
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 20 25 30

Ala Ser Thr Ala Asn Met Leu Arg Glu Gln Val Ala Gln Leu Lys Gln  
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Lys Val Met Asn His Gly Gly Cys Ala Ser Gly Gln Ala Gly Gln His  
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His His His His His Gly Ala Tyr Pro Tyr Asp Val Pro Asp Tyr Ala  
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Ser

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Leu Ala Ala Arg Ala Xaa Xaa Trp Gly Gln Gly Thr  
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<210> 61  
 <211> 18  
 <212> PRT  
 <213> artificial sequence

<220>  
 <223> TPO mimetic with flanking amino acids

<400> 61

Asn	Pro	Ile	Glu	Gly	Pro	Thr	Leu	Arg	Gln	Trp	Leu	Ala	Ala	Arg	Ala
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Arg Gly

<210> 62  
 <211> 41  
 <212> DNA  
 <213> artificial sequence



<220>  
 <223> primer  
  
 <400> 62  
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<210> 63  
 <211> 24  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer  
  
 <400> 63  
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<210> 64  
 <211> 24  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer  
  
 <400> 64  
 ccacgggcac agcctacatg gagc 24

<210> 65  
 <211> 54  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> nucleic acid encoding TPO mimetic peptide flanking sequence  
  
 <400> 65  
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<210> 66  
 <211> 18  
 <212> PRT  
 <213> artificial sequence

<220>  
 <223> TPO mimetic peptide with flanking sequence  
  
 <400> 66  
  
 Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
 1 5 10 15

Pro Val

<210> 67  
<211> 472  
<212> PRT  
<213> artificial sequence

<220>  
<223> Humanized antibody heavy chain

<400> 67

Met Lys Trp Ser Trp Val Ile Leu Phe Leu Leu Ser Val Thr Ala Gly  
1 5 10 15

Val His Ser Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys  
20 25 30

Pro Gly Ala Ser Val Lys Val Ser Cys Lys Ala Ser Gly Tyr Ile Phe  
35 40 45

Ser Asn Tyr Trp Ile Gln Trp Val Arg Gln Ala Pro Gly Gln Gly Leu  
50 55 60

Glu Trp Met Gly Glu Ile Leu Pro Gly Ser Gly Ser Thr Glu Tyr Thr  
65 70 75 80

Glu Asn Phe Lys Asp Arg Val Thr Met Thr Arg Asp Thr Ser Thr Ser  
85 90 95

Thr Val Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val  
100 105 110

Tyr Tyr Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp  
115 120 125

Leu Ala Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Leu Val Thr Val  
130 135 140

Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Cys  
145 150 155 160

Ser Arg Ser Thr Ser Glu Ser Thr Ala Ala Leu Gly Cys Leu Val Lys  
165 170 175

Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu  
180 185 190

Thr Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu  
195 200 205

Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser Ser Asn Phe Gly Thr  
210 215 220

Gln Thr Tyr Thr Cys Asn Val Asp His Lys Pro Ser Asn Thr Lys Val  
225 230 235 240

Asp Lys Thr Val Glu Arg Lys Cys Cys Val Glu Cys Pro Pro Cys Pro  
245 250 255

Ala Pro Pro Val Ala Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro  
260 265 270

Lys Asp Thr Leu Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val  
275 280 285

Val Asp Val Ser Gln Glu Asp Pro Glu Val Gln Phe Asn Trp Tyr Val  
290 295 300

Asp Gly Val Glu Val His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln  
305 310 315 320

Phe Asn Ser Thr Tyr Arg Val Val Ser Val Leu Thr Val Leu His Gln  
325 330 335

Asp Trp Leu Asn Gly Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Gly  
340 345 350

Leu Pro Ser Ser Ile Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro  
355 360 365

Arg Glu Pro Gln Val Tyr Thr Leu Pro Pro Ser Gln Glu Glu Met Thr  
370 375 380

Lys Asn Gln Val Ser Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser  
385 390 395 400

Asp Ile Ala Val Glu Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr  
405 410 415

Lys Thr Thr Pro Pro Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr  
420 425 430

Ser Arg Leu Thr Val Asp Lys Ser Arg Trp Gln Glu Gly Asn Val Phe  
435 440 445

Ser Cys Ser Val Met His Glu Ala Leu His Asn His Tyr Thr Gln Lys  
450 455 460

Ser Leu Ser Leu Ser Leu Gly Lys  
465 470

<210> 68  
<211> 1419  
<212> DNA  
<213> artificial sequence

<220>  
<223> nucleic acid encoding humanized antibody heavy chain

<400> 68  
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gaaaatttta aagaccgtgt tactatgacg cgtgacactt cgactagtac agtatacatg 300  
gagctctcca gctgcgatc ggaggacacg gccgtctatt attgcgcgcg tttgccaaatt 360  
gaagggccga cgctgcggca atggctggcg gcgcgcgcgc ctgtttgggg tcaaggaacc 420  
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 tacacacaga agagcctctc cctgtctctg ggtaaata 1419

<210> 69  
 <211> 236  
 <212> PRT  
 <213> artificial sequence

<220>  
 <223> Humanized antibody light chain

<400> 69

Met Asp Met Arg Val Pro Ala Gln Leu Leu Gly Leu Leu Leu Leu Trp  
 1 5 10 15

Leu Arg Gly Ala Arg Cys Asp Ile Gln Met Thr Gln Ser Pro Ser Ser  
 20 25 30

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Gly Ala Ser  
 35 40 45

Glu Asn Ile Tyr Gly Ala Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys  
 50 55 60

Ala Pro Lys Leu Leu Ile Tyr Gly Ala Thr Asn Leu Ala Asp Gly Val  
 65 70 75 80

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr  
 85 90 95

Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Asn

100	105	110
Val Leu Asn Thr Pro Leu Thr Phe Gly Gln Gly Thr Lys Val Glu Ile		
115	120	125
Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp		
130	135	140
Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn		
145	150	155
Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu		
165	170	175
Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp		
180	185	190
Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr		
195	200	205
Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser		
210	215	220
Ser Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys		
225	230	235

<210> 70  
 <211> 711  
 <212> DNA  
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<220>  
 <223> nucleic acid encoding humanized antibody light chain

<400> 70  
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 gtcaccatca cctgcggcgc cagcgaaaac atctatggcg cgctgaactg gtatcaacag 180  
 aaacccggga aagctccgaa gcttctgatt tacgggtgcga cgaacctggc agatggagtc 240  
 ccttctcgct tctctggatc cggctccgga acggatttca ctctgaccat cagcagtctg 300  
 cagcctgaag acttcgctac gtattactgt cagaacgttt taaatactcc gttgactttc 360  
 ggacagggta ccaaggtgga aataaaacga actgtggctg caccatctgt cttcatcttc 420

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ccgccatctg atgagcagtt gaaatctgga actgcctctg ttgtgtgcct gctgaataac 480
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ctgacgctga gcaaagcaga ctacgagaaa cacaaagtct acgcctgcga agtcacccat 660
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<210> 71
<211> 22
<212> PRT
<213> artificial sequence

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<220>
<223> EPO mimetic with random flanking amino acids

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<221> MISC_FEATURE
<222> (1)..(2)
<223> Xaa is any amino acid

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<220>
<221> MISC_FEATURE
<222> (6)..(6)
<223> Xaa is any amino acid

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<220>
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<223> Xaa is any amino acid

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<220>
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<222> (21)..(22)
<223> Xaa is any amino acid

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<400> 71

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Xaa Xaa Asp Tyr His Xaa Arg Met Gly Pro Leu Thr Trp Val Xaa Lys
1           5           10           15

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Pro Leu Gly Gly Xaa Xaa
20

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<210> 72
<211> 21
<212> DNA
<213> artificial sequence

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<220>

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<223> primer  
 <400> 72  
 taggatgcgg ccgcacaggt c 21

<210> 73  
 <211> 39  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 73  
 cacgcgcaca acacgtctag araccatccag atgacccag 39

<210> 74  
 <211> 39  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 74  
 cacgcgcaca acacgtctag agmccatccag ttgacccag 39

<210> 75  
 <211> 39  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 75  
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<210> 76  
 <211> 39  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 76  
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<210> 77  
 <211> 39  
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<213> artificial sequence  
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 <400> 77  
 cacgcgcaca acacgtctag agatattgtg atgacccag 39

<210> 78  
 <211> 39  
 <212> DNA  
 <213> artificial sequence  
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 <400> 78  
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<210> 79  
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<210> 80  
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 <400> 80  
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<210> 81  
 <211> 39  
 <212> DNA  
 <213> artificial sequence  
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 <223> primer  
 <400> 81  
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<210> 82  
<211> 39  
<212> DNA  
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<220>  
<223> primer

<400> 82  
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39

<210> 83  
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<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 83  
cacgcgaca acacgtctag agaaacgaca ctcacgcag

39

<210> 84  
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<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 84  
cacgcgaca acacgtctag agaaattgtg ctgactcag

39

<210> 85  
<211> 39  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 85  
cacgcgaca acacgtctag agatgttgtg atgacacag

39

<210> 86  
<211> 22  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 86

attaatacga ctcactatag gg 22

<210> 87  
 <211> 20  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 87  
 aattaaccct cactaaaggg 20

<210> 88  
 <211> 59  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 88  
 agccagccac tggcgcaggg ttgggccttc gatcgggttc ctgatgagga gctttggrg 59

<210> 89  
 <211> 59  
 <212> DNA  
 <213> artificial sequence

<220>  
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<400> 89  
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<210> 90  
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<220>  
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<400> 90  
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<210> 91  
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 <212> DNA  
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<220>

<223> primer

<400> 91  
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<210> 92  
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<210> 93  
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 <212> PRT  
 <213> artificial sequence

<220>  
 <223> part of mimetic

<400> 112

Gly Pro Thr Leu Arg Gln Trp Leu  
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<210> 113  
 <211> 18  
 <212> PRT  
 <213> artificial sequence

<220>  
 <223> artificial CDR2

<220>  
 <221> MISC\_FEATURE  
 <222> (2)..(2)  
 <223> Xaa is any amino acid

<220>  
 <221> MISC\_FEATURE  
 <222> (11)..(11)  
 <223> Xaa is any amino acid

<400> 113

Gly Xaa Gly Pro Thr Leu Arg Gln Trp Leu Xaa Tyr Ala Gln Lys Phe  
 1 5 10 15

Gln Gly

<210> 114

<211> 48  
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<220>  
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<220>  
 <221> misc\_feature  
 <222> (26)..(27)  
 <223> n is a, c, g or t

<400> 114  
 cagccactgg cgcagggttg ggccmnnccc tcccatccac tcaagccc 48

<210> 115  
 <211> 60  
 <212> DNA  
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<220>  
 <223> primer

<220>  
 <221> misc\_feature  
 <222> (25)..(26)  
 <223> n is a, c, g or t

<400> 115  
 ggccaaccc tgcgccagtg gctgnnktac gcacagaaat tccagggcag agtcaccatt 60

<210> 116  
 <211> 354  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> nucleotides encoding variable region of light chain

<400> 116  
 gacatccaga tgaccagtc tccatcctcc ctgtctgcat ctgtaggaga cagagtcacc 60  
 atcacttgcc gggcgagtca gagtattagt agtttgctgg cctgggtatca gcagaaacca 120  
 gggaaagctc ctaagctcct gatctataac ccgatcgaag gccaaccct gcgccagtgg 180  
 ctggctactc gcgctcgtgg tgggggtcca tcaagggtca gcggcagtgg atctgggaca 240  
 gatttcactc tcaccatcag cagcctgcag cctgaagatt ttgcaactta ttactgccaa 300  
 cagtataata gttaccctcc cactttcggc cctgggacca aagtggatat caaa 354

<210> 117  
 <211> 233  
 <212> PRT  
 <213> human

<400> 117

Glu Val Gln Leu Leu Glu Gln Ser Gly Ala Glu Val Lys Lys Pro Gly  
 1 5 10 15

Ser Ser Val Lys Val Ser Cys Arg Ala Ser Gly Gly Thr Phe Asn Asn  
 20 25 30

Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp  
 35 40 45

Met Gly Gly Ile Phe Pro Phe Arg Asn Thr Ala Lys Tyr Ala Gln His  
 50 55 60

Phe Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Gly Thr Ala  
 65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile Tyr Tyr  
 85 90 95

Cys Ala Arg Gly Asp Thr Ile Phe Gly Val Thr Met Gly Tyr Tyr Ala  
 100 105 110

Met Asp Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ala Ala Ser  
 115 120 125

Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr  
 130 135 140

Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro  
 145 150 155 160

Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val  
 165 170 175

His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser  
 180 185 190

Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile  
 195 200 205

Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys Lys Val  
 210 215 220

Glu Pro Lys Ser Cys Asp Lys Thr Ser  
 225 230

<210> 118  
 <211> 212  
 <212> PRT  
 <213> human

<400> 118

Glu Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg  
 1 5 10 15

Ala Thr Leu Ser Cys Arg Ala Ser His Ser Val Ser Arg Ala Tyr Leu  
 20 25 30

Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr  
 35 40 45

Gly Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser  
 50 55 60

Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu  
 65 70 75 80

Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Gly Ser Pro Trp Phe  
 85 90 95

Gly Gln Gly Thr Lys Val Glu Leu Lys Arg Thr Val Ala Ala Pro Ser  
 100 105 110

Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala  
 115 120 125

Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val  
 130 135 140

Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser  
 145 150 155 160

Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr  
165 170 175

Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys  
180 185 190

Glu Val Thr His Gln Gly Leu Ser Leu Pro Val Thr Lys Ser Phe Asn  
195 200 205

Arg Gly Glu Cys  
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<210> 119  
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<212> PRT  
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<220>  
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<220>  
<221> MISC\_FEATURE  
<222> (4)..(5)  
<223> Xaa can be any naturally occurring amino acid

<220>  
<221> MISC\_FEATURE  
<222> (20)..(21)  
<223> Xaa can be any naturally occurring amino acid

<400> 119

Gly Ile Phe Xaa Xaa Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
1 5 10 15

Ala Arg Ala Xaa Xaa Gly  
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<210> 120  
<211> 60  
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<220>  
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<220>  
<221> misc\_feature  
<222> (35)..(36)

<223> n is a, c, g or t

<220>

<221> misc\_feature

<222> (38)..(39)

<223> n is a, c, g or t

<400> 120

agccagccac tggcgcaggg ttgggccttc gatmnnmnnng aagatccctc ccatccactc 60

<210> 121

<211> 60

<212> DNA

<213> artificial sequence

<220>

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<220>

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<222> (34)..(35)

<223> n is a, c, g or t

<220>

<221> misc\_feature

<222> (37)..(38)

<223> n is a, c, g or t

<400> 121

ccaaccctgc gccagtggct ggctgctcgc gctnnknnkg gcagagtcac cattaccgcg 60

<210> 122

<211> 215

<212> PRT

<213> artificial sequence

<220>

<223> antibody light chain

<400> 122

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly  
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser  
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu  
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser



50

55

60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu  
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro  
85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala  
100 105 110

Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser  
115 120 125

Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu  
130 135 140

Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser  
145 150 155 160

Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu  
165 170 175

Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val  
180 185 190

Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Leu Pro Val Thr Lys  
195 200 205

Ser Phe Asn Arg Gly Glu Cys  
210 215

<210> 123

<211> 108

<212> PRT

<213> artificial sequence

<220>

<223> antibody light chain variable region

<400> 123

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly  
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser  
 20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu  
 35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser  
 50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu  
 65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro  
 85 90 95

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
 100 105

<210> 124

<211> 249

<212> PRT

<213> artificial sequence

<220>

<223> antibody heavy chain

<400> 124

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr  
 20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
 35 40 45

Gly Gln Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg  
 50 55 60

Ala Asn Ser Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala  
 65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr  
 85 90 95

Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
100 105 110

Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
115 120 125

Ala Ser Thr Lys Gly Pro Ser Val Phe Pro Leu Ala Pro Ser Ser Lys  
130 135 140

Ser Thr Ser Gly Gly Thr Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr  
145 150 155 160

Phe Pro Glu Pro Val Thr Val Ser Trp Asn Ser Gly Ala Leu Thr Ser  
165 170 175

Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser  
180 185 190

Leu Ser Ser Val Val Thr Val Pro Ser Ser Ser Leu Gly Thr Gln Thr  
195 200 205

Tyr Ile Cys Asn Val Asn His Lys Pro Ser Asn Thr Lys Val Asp Lys  
210 215 220

Lys Val Glu Pro Lys Ser Cys Asp Lys Thr His Thr Cys Pro Pro Cys  
225 230 235 240

Pro Ala Pro Glu Leu Leu Gly Gly Pro  
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<210> 125

<211> 128

<212> PRT

<213> artificial sequence

<220>

<223> antibody heavy chain variable region

<400> 125

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr  
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Gln Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg  
50 55 60

Ala Asn Ser Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala  
65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr  
85 90 95

Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
100 105 110

Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
115 120 125

<210> 126  
<211> 22  
<212> PRT  
<213> artificial sequence

<220>  
<223> heavy chain CDR2 clone

<220>  
<221> MISC\_FEATURE  
<222> (4)..(5)  
<223> Xaa can be any naturally occurring amino acid

<220>  
<221> MISC\_FEATURE  
<222> (20)..(21)  
<223> Xaa can be any naturally occurring amino acid

<400> 126

Gly Ile Phe Xaa Xaa Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
1 5 10 15

Ala Arg Ala Xaa Xaa Gly  
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<210> 127  
<211> 22

<212> PRT  
<213> artificial sequence

<220>  
<223> heavy chain CDR2 clone

<400> 127

Gly Ile Phe Ser Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
1 5 10 15

Ala Arg Ala Ala Gly Gly  
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<210> 128  
<211> 22  
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<220>  
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<400> 128

Gly Ile Phe Pro Gln Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
1 5 10 15

Ala Arg Ala Lys His Gly  
20

<210> 129  
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<400> 129

Gly Ile Phe Pro Asn Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
1 5 10 15

Ala Arg Ala Thr Gly Gly  
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<210> 130  
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 Gly Ile Phe Lys Gly Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
 1 5 10 15

Ala Arg Ala Pro Gly Gly  
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<210> 131  
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<400> 131  
 Gly Ile Phe Pro Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
 1 5 10 15

Ala Arg Ala Ala Val Gly  
 20

<210> 132  
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<400> 132  
 Gly Ile Phe Pro Arg Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
 1 5 10 15

Ala Arg Ala Lys Leu Gly  
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<210> 133  
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<220>  
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<400> 133

Gly Ile Phe Pro Arg Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
1 5 10 15

Ala Arg Ala Lys Leu Gly  
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<210> 134

<211> 22

<212> PRT

<213> artificial sequence

<220>

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<400> 134

Gly Ile Phe Pro Tyr Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
1 5 10 15

Ala Arg Ala Lys Arg Gly  
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<210> 135

<211> 42

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 135

gacgcgcaca acacggagct cgaaattgtg ctgacccaga gc

42

<210> 136

<211> 44

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 136

agacagttag cgccgtctag aattagcatt cgccgcggtt aaag

44

<210> 137

<211> 36

<212> DNA

<213> artificial sequence

<220>  
 <223> primer

<400> 137  
 gacgcgcaca acacggggccc gagcgtgttt ccgctg 36

<210> 138  
 <211> 41  
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<220>  
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<400> 138  
 agacagttag cgccgactag ttttatcgca gcttttcggt t 41

<210> 139  
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<400> 139  
 gagccgcacg agcccctcga gcaggtgcag ctggtgcaga g 41

<210> 140  
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<220>  
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<400> 140  
 gcaaagtgtg aggggccctt ggtgctcgcg ctgct 35

<210> 141  
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<220>  
 <223> expression vector

<400> 141  
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agatagggtt gagtgttggt ccagtttggg acaagagtcc actattaaag aacgtggact 180



ccaacgtcaa agggcgaaaa accgtctatc agggcgatgg ccactacgt gaaccatcac	240
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ccacacccgc cgcgcttaat gcgcgctac agggcgcgctc aggtggcact tttcggggaa	480
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<210> 142

<211> 239

<212> PRT

<213> artificial sequence

<220>

<223> recombinant Ab light chain

<400> 142

Met	Lys	Lys	Thr	Ala	Ile	Ala	Ile	Ala	Val	Ala	Leu	Ala	Gly	Phe	Ala
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Thr Val Ala Gln Ala Ala Glu Leu Glu Ile Val Leu Thr Gln Ser Pro

20

25

30

Gly Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg  
 35 40 45

Ala Ser Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys  
 50 55 60

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala  
 65 70 75 80

Thr Gly Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe  
 85 90 95

Thr Leu Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr  
 100 105 110

Cys Gln Gln Tyr Gly Ser Ser Pro Trp Thr Phe Gly Gln Gly Thr Lys  
 115 120 125

Val Glu Ile Lys Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro  
 130 135 140

Pro Ser Asp Glu Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu  
 145 150 155 160

Leu Asn Asn Phe Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp  
 165 170 175

Asn Ala Leu Gln Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp  
 180 185 190

Ser Lys Asp Ser Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys  
 195 200 205

Ala Asp Tyr Glu Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln  
 210 215 220

Gly Leu Ser Leu Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys  
 225 230 235

<210> 143

<211> 282

<212> PRT  
<213> artificial sequence

<220>  
<223> recombinant Ab heavy chain

<400> 143

Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala  
1 5 10 15

Ala Gln Pro Ala Met Ala Leu Glu Gln Val Gln Leu Val Gln Ser Gly  
20 25 30

Ala Glu Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala  
35 40 45

Ser Gly Gly Thr Phe Ser Ser Tyr Ala Ile Ser Trp Val Arg Gln Ala  
50 55 60

Pro Gly Gln Gly Leu Glu Trp Met Gly Gln Leu Ile Glu Gly Pro Thr  
65 70 75 80

Leu Arg Gln Trp Leu Ala Ala Arg Ala Asn Ser Arg Val Thr Ile Thr  
85 90 95

Ala Asp Glu Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg  
100 105 110

Ser Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg Leu Pro Ile Glu Gly  
115 120 125

Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala Pro Val Trp Gly Gln  
130 135 140

Gly Thr Thr Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val  
145 150 155 160

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala  
165 170 175

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser  
180 185 190

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val

195                      200                      205  
 Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro  
     210                      215                      220  
 Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys  
 225                      230                      235                      240  
 Pro Ser Asn Thr Lys Val Asp Lys Lys Val Glu Pro Lys Ser Cys Asp  
                     245                      250                      255  
 Lys Thr Ser Gly Gln Ala Gly Gln His His His His His His Gly Ala  
                     260                      265                      270  
 Tyr Pro Tyr Asp Val Pro Asp Tyr Ala Ser  
                     275                      280

<210> 144  
 <211> 24  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 144  
 aaaggtgccg ccgctcgctt tgca

24

<210> 145  
 <211> 42  
 <212> DNA  
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<220>  
 <223> primer

<220>  
 <221> misc\_feature  
 <222> (13)..(14)  
 <223> n is a, c, g or t

<220>  
 <221> misc\_feature  
 <222> (16)..(17)  
 <223> n is a, c, g or t

<400> 145  
 ggcggcacct tttnknkta tgcgattagc tgggtgcgcc ag

42

<210> 146  
<211> 42  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 146  
ggcggcacct ttaacaacta tgcgattagc tgggtgcgcc ag

42

<210> 147  
<211> 128  
<212> PRT  
<213> artificial sequence

<220>  
<223> cloned antibody VH

<400> 147

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr  
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Gln Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg  
50 55 60

Ala Asn Ser Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala  
65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr  
85 90 95

Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
100 105 110

Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
115 120 125

<210> 148  
<211> 128

<212> PRT  
<213> artificial sequence

<220>  
<223> cloned antibody VH

<400> 148

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Asn Asn Tyr  
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Gln Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg  
50 55 60

Ala Asn Ser Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala  
65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr  
85 90 95

Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
100 105 110

Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
115 120 125

<210> 149  
<211> 128  
<212> PRT  
<213> artificial sequence

<220>  
<223> cloned antibody VH

<400> 149

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Gly Glu Tyr  
20 25 30



Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
 35 40 45

Gly Gln Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg  
 50 55 60

Ala Asn Ser Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala  
 65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr  
 85 90 95

Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
 100 105 110

Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
 115 120 125

<210> 150  
 <211> 128  
 <212> PRT  
 <213> artificial sequence

<220>  
 <223> cloned antibody VH

<400> 150

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
 1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Gln Asp Tyr  
 20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
 35 40 45

Gly Gln Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg  
 50 55 60

Ala Asn Ser Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala  
 65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr  
 85 90 95

Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
100 105 110

Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
115 120 125

<210> 151  
<211> 128  
<212> PRT  
<213> artificial sequence

<220>  
<223> cloned antibody VH

<400> 151

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Pro Arg Tyr  
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Gln Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg  
50 55 60

Ala Asn Ser Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala  
65 70 75 80

Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr  
85 90 95

Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala  
100 105 110

Ala Arg Ala Pro Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ser  
115 120 125

<210> 152  
<211> 18  
<212> PRT  
<213> artificial sequence

<220>

<223> flanked TPO mimetic

<400> 152

Gln Leu Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala Arg Ala  
1 5 10 15

Asn Ser

<210> 153

<211> 871

<212> DNA

<213> human

<400> 153

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taacaaccac attcctcctc taaagaagcc cctgggagca cagctcatca ccatggactg 240  
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ggcagctgtg ccgggctgag gagatgacag ggtttattag gtttaaggct gtttacaaaa 780  
tgggttatat atttgagaaa aaaagaacag tagaaacaag tacatactcc tctaatttta 840  
agataattat tccattcaag agtcgtaata t 871

<210> 154

<211> 20

<212> PRT

<213> human

<400> 154

Tyr Tyr Tyr Tyr Tyr Gly Met Asp Val Trp Gly Gln Gly Thr Thr Val  
 1 5 10 15

Thr Val Ser Ser  
 20

<210> 155  
 <211> 711  
 <212> DNA  
 <213> human

<400> 155  
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 gcatgtcagt gaaaaccctc tcaagtctg ttacctggca actctgctca gtcaatacaa 240  
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 gtgttgacgc agtctccagg caccctgtct ttgtctccag gggaaagagc caccctctcc 420  
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 gattttgcag tgtattactg tcagcagtat ggtagctcac ctcccacagt gattcagctt 660  
 gaaacaaaaa cctctgcaag accttcattg ttactagat tataccagct g 711

<210> 156  
 <211> 12  
 <212> PRT  
 <213> human

<400> 156

Trp Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys  
 1 5 10

<210> 157  
 <211> 447  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> recombinant DNA encoding AB VH

<400> 157  
atgaaatacc tattgcctac ggcagccgct ggattgttat tactcgctgc ccaaccagcc 60  
atggcgcagg tgcagctggg gcagagcggc gcggaagtga aaaaaggcag cagcgtgaaa 120  
gtgagctgca aagcgagcgg cggcaccttt agcagctatg cgattagctg ggtgcgccag 180  
gcgccggggc agggcctgga atggatgggc cagctgattg aaggcccgac cctgcgccag 240  
tggctggcgg cgcgcgcgaa cagccgcgtg accattaccg cggatgaaag caccagcacc 300  
gcgtatatgg aactgagcag cctgcgcagc gaagataccg cgggtgtatta ttgcgcgcgc 360  
ctgccgattg aaggcccgac cctgcgccag tggctggcgg cgcgcgcgcc ggtgtggggc 420  
cagggcacca ccgtgaccgt gagcagc 447

<210> 158  
<211> 150  
<212> PRT  
<213> artificial sequence

<220>  
<223> recombinant Ab VH

<400> 158

Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala  
1 5 10 15

Ala Gln Pro Ala Met Ala Gln Val Gln Leu Val Gln Ser Gly Ala Glu  
20 25 30

Val Lys Lys Pro Gly Ser Ser Val Lys Val Ser Cys Lys Ala Ser Gly  
35 40 45

Gly Thr Phe Ser Ser Tyr Ala Ile Ser Trp Val Arg Gln Ala Pro Gly  
50 55 60

Gln Gly Leu Glu Trp Met Gly Gln Leu Ile Glu Gly Pro Thr Leu Arg  
65 70 75 80

Gln Trp Leu Ala Ala Arg Ala Asn Ser Arg Val Thr Ile Thr Ala Asp  
85 90 95

Glu Ser Thr Ser Thr Ala Tyr Met Glu Leu Ser Ser Leu Arg Ser Glu  
100 105 110

Asp Thr Ala Val Tyr Tyr Cys Ala Arg Leu Pro Ile Glu Gly Pro Thr  
115 120 125

Leu Arg Gln Trp Leu Ala Ala Arg Ala Pro Val Trp Gly Gln Gly Thr  
130 135 140

Thr Val Thr Val Ser Ser  
145 150

<210> 159  
<211> 127  
<212> PRT  
<213> artificial sequence

<220>  
<223> recombinant Ab VH

<400> 159

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
1 5 10 15

Ser Val Lys Val Ser Cys Arg Ala Ser Gly Gly Thr Phe Asn Asn Tyr  
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Gly Ile Phe Pro Phe Arg Asn Thr Ala Lys Tyr Ala Gln His Phe  
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Gly Thr Ala Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Ile Tyr Tyr Cys  
85 90 95

Ala Arg Leu Pro Ile Glu Gly Pro Thr Leu Arg Gln Trp Leu Ala Ala  
100 105 110

Arg Ala Pro Val Trp Gly Gln Gly Thr Thr Val Thr Val Ser Ala  
115 120 125

<210> 160  
<211> 390  
<212> DNA

<213> artificial sequence

<220>

<223> recombinant DNA encoding Ab Vk

<400> 160

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atgaaatacc tattgcctac ggcagccgct ggattgttat tactcgctgc ccaaccagcc      60
atggcgggaaa ttgtgctgac ccagagcccg ggcaccctga gcctgagccc gggcgaacgc      120
gcgaccctga gctgccgcgc gagccagagc gtgagcagca gctatctggc gtggtatcag      180
cagaaaccgg gccaggcgcc gcgcctgctg atttatggcg cgagcagccg cgcgaccggc      240
attccggatc gcttttagcgg cagcggcagc ggcaccgatt ttaccctgac cattagccgc      300
ctggaaccgg aagattttgc ggtgtattat tgccagcagt atggcagcag cccgtggacc      360
tttgcccagg gcaccaaagt ggaaattaa                                     390
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<210> 161

<211> 130

<212> PRT

<213> artificial sequence

<220>

<223> recombinant Ab Vk

<400> 161

```
Met Lys Tyr Leu Leu Pro Thr Ala Ala Ala Gly Leu Leu Leu Leu Ala
1           5           10           15
```

```
Ala Gln Pro Ala Met Ala Glu Ile Val Leu Thr Gln Ser Pro Gly Thr
20           25           30
```

```
Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser
35           40           45
```

```
Gln Ser Val Ser Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly
50           55           60
```

```
Gln Ala Pro Arg Leu Leu Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly
65           70           75           80
```

```
Ile Pro Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu
85           90           95
```

```
Thr Ile Ser Arg Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln
100          105          110
```

Gln Tyr Gly Ser Ser Pro Trp Thr Phe Gly Gln Gly Thr Lys Val Glu  
115 120 125

Ile Lys  
130

<210> 162  
<211> 107  
<212> PRT  
<213> artificial sequence

<220>  
<223> recombinant Ab Vk

<400> 162

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly  
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser His Ser Val Ser Arg Ala  
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu  
35 40 45

Ile Tyr Gly Thr Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser  
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu  
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Gly Ser Pro  
85 90 95

Trp Phe Gly Gln Gly Thr Lys Val Glu Leu Lys  
100 105

<210> 163  
<211> 272  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 163



ccagccatgg cgcaggtgca gctggtgcag agcggcgcgg aagtgaaaa accgggcagc 60  
agcgtgaaag tgagctgcaa agcgagcggc ggcaccttta gcagctatgc gattagctgg 120  
gtgcgccagg cgccggggcca gggcctggaa tggatgggcg gcattattcc gatttttggc 180  
accgcgaact atgcgcagaa atttcagggc cgcgtgacca ttaccgcgga tgaaagcacc 240  
agcaccgcgt atatggaact gagcagcctg cg 272

<210> 164  
<211> 271  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 164  
gttccagctc acggtcaccg gttccggaaa ataatctttc accaggcagc ccagcgccgc 60  
ggcgccgcgc ctggtgcttt tgctgctcgg cgccagcggg aacacgctcg ggcctttggt 120  
gctcgcgctg ctcacgggtc cgggtggtgcc ctggcccccac accggcgcgcg gcgcgcgcag 180  
ccactggcgc agggctcgggc cttcaatcgg caggcgcgcg caataatata ccgcgggtatc 240  
ttcgctgcgc aggctgctca gttccatata c 271

<210> 165  
<211> 274  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 165  
cgagtctaga ttacgggccg ccagcagtt ccggcgccgg gcacggcggg caggtatggg 60  
ttttatcgca gcttttcggg tccacttttt tatccacttt ggtggtgctc ggtttatggt 120  
tcacgttgca aatataggtc tgggtgccca ggctgctgct cggcacgggtc accacgctgc 180  
tcaggctata caggcgctg ctctgcagca ccgcgggaaa ggtatgcacg ccgctgggtca 240  
gcgcgcgcgt gttccagctc acggtcaccg gttc 274

<210> 166  
<211> 236  
<212> DNA  
<213> artificial sequence

<220>

<223> primer

<400> 166

ccagccatgg cggaaattgt gctgacctag agcccgggca ccctgagcct gagccccggc 60  
gaacgcgcga ccctgagctg ccgcgcgagc cagagcgtga gcagcagcta tctggcgtgg 120  
tatcagcaga aaccggggcca ggcgcgcgcg ctgctgattt atggcgcgag cagccgcgcg 180  
accggcattc cggatcgctt tagcggcagc ggcagcggca ccgattttac cctgac 236

<210> 167

<211> 238

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 167

ctttcgcttc gcgcggataa aagttgttca gcaggcacac cacgctcgcg gtgccgcttt 60  
tcagtgttca tcgctcggcg gaaaaataaa cacgctcggc gccgccacgg tgcgtttaat 120  
ttccactttg gtgccttggc caaagggtcca cgggctgctg ccatactgct ggcaataata 180  
caccgcaaaa tottccggtt ccaggcgggt aatggtcagg gtaaaatcgg tgccgctg 238

<210> 168

<211> 245

<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 168

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gatgggtcac ttgcacgca tacactttat gtttttcata atccgctttg ctcagggtca 120  
gggtgctgct caggctatag gtgctatctt tgctatcctg ttcggtcacg ctttcctggc 180  
tgttgcgct ctgcagcgcg ttatocactt tccactgcac ttctgcttcg cgcggataaa 240  
agttg 245

<210> 169

<211> 98

<212> PRT

<213> artificial sequence

<220>

<223> recombinant Ab VH

<400> 169

Gln Val Gln Leu Val Gln Ser Gly Ala Glu Val Lys Lys Pro Gly Ser  
1 5 10 15

Ser Val Lys Val Ser Cys Lys Ala Ser Gly Gly Thr Phe Ser Ser Tyr  
20 25 30

Ala Ile Ser Trp Val Arg Gln Ala Pro Gly Gln Gly Leu Glu Trp Met  
35 40 45

Gly Gly Ile Ile Pro Ile Phe Gly Thr Ala Asn Tyr Ala Gln Lys Phe  
50 55 60

Gln Gly Arg Val Thr Ile Thr Ala Asp Glu Ser Thr Ser Thr Ala Tyr  
65 70 75 80

Met Glu Leu Ser Ser Leu Arg Ser Glu Asp Thr Ala Val Tyr Tyr Cys  
85 90 95

Ala Arg

<210> 170

<211> 96

<212> PRT

<213> human

<400> 170

Glu Ile Val Leu Thr Gln Ser Pro Gly Thr Leu Ser Leu Ser Pro Gly  
1 5 10 15

Glu Arg Ala Thr Leu Ser Cys Arg Ala Ser Gln Ser Val Ser Ser Ser  
20 25 30

Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu  
35 40 45

Ile Tyr Gly Ala Ser Ser Arg Ala Thr Gly Ile Pro Asp Arg Phe Ser  
50 55 60

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Arg Leu Glu  
65 70 75 80

Pro Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Tyr Gly Ser Ser Pro  
85 90 95

<210> 171  
<211> 177  
<212> PRT  
<213> artificial sequence

<220>  
<223> recombinant Ab heavy chain

<400> 171

Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu Gly Gly Gly Ser Glu  
1 5 10 15

Gly Gly Gly Ser Gly Gly Gly Ser Gly Ser Gly Asp Phe Asp Tyr Glu  
20 25 30

Lys Met Ala Asn Ala Asn Lys Gly Ala Met Thr Glu Asn Ala Asp Glu  
35 40 45

Asn Ala Leu Gln Ser Asp Ala Lys Gly Lys Leu Asp Ser Val Ala Thr  
50 55 60

Asp Tyr Gly Ala Ala Ile Asp Gly Phe Ile Gly Asp Val Ser Gly Leu  
65 70 75 80

Ala Asn Gly Asn Gly Ala Thr Gly Asp Phe Ala Gly Ser Asn Ser Gln  
85 90 95

Met Ala Gln Val Gly Asp Gly Asp Asn Ser Pro Leu Met Asn Asn Phe  
100 105 110

Arg Gln Tyr Leu Pro Ser Leu Pro Gln Ser Val Glu Cys Arg Pro Phe  
115 120 125

Val Phe Ser Ala Gly Lys Pro Tyr Glu Phe Ser Ile Asp Cys Asp Lys  
130 135 140

Ile Asn Leu Phe Arg Gly Val Phe Ala Phe Leu Leu Tyr Val Ala Thr  
145 150 155 160

Phe Met Tyr Val Phe Ser Thr Phe Ala Asn Ile Leu Arg Asn Lys Glu  
165 170 175

Ser

<210> 172  
<211> 17  
<212> PRT  
<213> human

<400> 172

Cys Phe Gly Arg Lys Met Asp Arg Ile Ser Ser Ser Ser Gly Leu Gly  
1 5 10 15

Cys

<210> 173  
<211> 39  
<212> PRT  
<213> human

<400> 173

His Gly Glu Gly Arg Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu  
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser  
20 25 30

Ser Gly Ala Pro Pro Pro Ser  
35

<210> 174  
<211> 30  
<212> PRT  
<213> human

<400> 174

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly  
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg  
20 25 30

<210> 175  
<211> 34

<212> PRT  
<213> human

<400> 175

His Ala Asp Gly Ser Phe Ser Asp Glu Met Asn Thr Ile Leu Asp Asn  
1 5 10 15

Leu Ala Ala Arg Asp Phe Ile Asn Trp Leu Ile Gln Thr Lys Ile Thr  
20 25 30

Asp Arg

<210> 176  
<211> 29  
<212> PRT  
<213> human

<400> 176

His Ser Gln Gly Thr Phe Thr Ser Asp Tyr Ser Lys Tyr Leu Asp Ser  
1 5 10 15

Arg Arg Ala Gln Asp Arg Val Gln Trp Leu Met Asn Thr  
20 25

<210> 177  
<211> 38  
<212> PRT  
<213> human

<400> 177

His Ser Asp Gly Ile Phe Thr Asp Ser Tyr Ser Arg Tyr Arg Lys Gln  
1 5 10 15

Met Ala Val Lys Lys Tyr Leu Ala Ala Val Leu Gly Lys Arg Tyr Lys  
20 25 30

Gln Arg Val Lys Asn Lys  
35

<210> 178  
<211> 130  
<212> PRT  
<213> human

<400> 178

Phe Ser Val Gly Leu Glu Thr Tyr Val Thr Ile Pro Asn Met Pro Ile  
 1 5 10 15

Arg Phe Thr Lys Ile Phe Tyr Asn Gln Gln Asn His Tyr Asp Gly Ser  
 20 25 30

Thr Gly Lys Phe His Cys Asn Ile Pro Gly Leu Tyr Tyr Phe Ala Tyr  
 35 40 45

His Ile Thr Val Tyr Met Lys Asp Val Lys Val Ser Leu Phe Lys Lys  
 50 55 60

Asp Lys Ala Met Leu Phe Thr Tyr Asp Gln Tyr Gln Glu Asn Asn Val  
 65 70 75 80

Asp Gln Ala Ser Gly Ser Val Leu Leu His Leu Glu Val Gly Asp Gln  
 85 90 95

Val Trp Leu Gln Val Tyr Gly Glu Gly Glu Arg Asn Gly Leu Tyr Ala  
 100 105 110

Asp Asn Asp Asn Asp Ser Thr Phe Thr Gly Phe Leu Leu Tyr His Asp  
 115 120 125

Thr Asn  
 130

<210> 179  
 <211> 21  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 179  
 gctgccaac cagccatggc c

21

<210> 180  
 <211> 23  
 <212> DNA  
 <213> artificial sequence

<220>  
 <223> primer

<400> 180  
atcaaaatca ccggaaccag agc 23

<210> 181  
<211> 72  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<220>  
<221> misc\_feature  
<222> (47)..(48)  
<223> n is a, c, g, or t

<220>  
<221> misc\_feature  
<222> (50)..(51)  
<223> n is a, c, g, or t

<400> 181  
ttccaaataa gaacttacat cactggtaaa ggtcccttca gcatgmnnmn ntctgcaca 60  
ataatatatg gc 72

<210> 182  
<211> 72  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<220>  
<221> misc\_feature  
<222> (46)..(47)  
<223> n is a, c, g, or t

<220>  
<221> misc\_feature  
<222> (49)..(50)  
<223> n is a, c, g, or t

<400> 182  
ggccaagctg ccaaggaatt cattgcttgg ctggtgaaag gccgannknn ktggggccaa 60  
gggaccacgg tc 72

<210> 183  
<211> 50  
<212> DNA



<213> artificial sequence  
 <220>  
 <223> primer  
 <400> 183  
 cagtgatgta agttcttatt tggaaggcca agctgccaag gaattcattg 50  
 <210> 184  
 <211> 50  
 <212> DNA  
 <213> artificial sequence  
 <220>  
 <223> primer  
 <400> 184  
 caatgaattc cttggcagct tggccttcca aataagaact tacatcactg 50  
 <210> 185  
 <211> 24  
 <212> DNA  
 <213> artificial sequence  
 <220>  
 <223> primer  
 <400> 185  
 tatgccatca gctgggtgcg acag 24  
 <210> 186  
 <211> 48  
 <212> DNA  
 <213> artificial sequence  
 <220>  
 <223> primer  
 <220>  
 <221> misc\_feature  
 <222> (23)..(24)  
 <223> n is a, c, g, or t  
 <220>  
 <221> misc\_feature  
 <222> (26)..(27)  
 <223> n is a, c, g, or t  
 <400> 186  
 tcgcacccag ctgatggcat amnnmnngaa ggtgcctcca gaagccct 48  
 <210> 187

<211> 23  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<400> 187  
atcaaaatca ccggaaccag agc

23

<210> 188  
<211> 65  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<220>  
<221> misc\_feature  
<222> (40)..(41)  
<223> n is a, c, g, or t

<220>  
<221> misc\_feature  
<222> (43)..(44)  
<223> n is a, c, g, or t

<400> 188  
ctctgggctc caatcctgtc catcctgccc ccgaagcamn nmnnctctgc acaataatat

60

atggc

65

<210> 189  
<211> 65  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<220>  
<221> misc\_feature  
<222> (39)..(40)  
<223> n is a, c, g, or t

<220>  
<221> misc\_feature  
<222> (42)..(43)  
<223> n is a, c, g, or t

<400> 189  
ggatggacag gattggagcc cagagcggac tgggctgtnn knnktggggc caagggacca

60

cggtc 65

<210> 190  
<211> 65  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<220>  
<221> misc\_feature  
<222> (40)..(41)  
<223> n is a, c, g, or t

<220>  
<221> misc\_feature  
<222> (43)..(44)  
<223> n is a, c, g, or t

<400> 190  
ctggaggagc tgatccggtc catcttcttc ccaaagcamn nmntctcgc acaataatat 60

atggc 65

<210> 191  
<211> 65  
<212> DNA  
<213> artificial sequence

<220>  
<223> primer

<220>  
<221> misc\_feature  
<222> (39)..(40)  
<223> n is a, c, g, or t

<220>  
<221> misc\_feature  
<222> (42)..(43)  
<223> n is a, c, g, or t

<400> 191  
agatggaccg gatcagctcc tccagtggcc tgggctgcnn knnktggggc caagggacca 60

cggtc 65

<210> 192  
<211> 24  
<212> DNA

<213> artificial sequence

<220>

<223> primer

<400> 192

tatgccatca gctgggtgcg acag

24

<210> 193

<211> 48

<212> DNA

<213> artificial sequence

<220>

<223> primer

<220>

<221> misc\_feature

<222> (23)..(24)

<223> n is a, c, g, or t

<220>

<221> misc\_feature

<222> (26)..(27)

<223> n is a, c, g, or t

<400> 193

tcgcaccag ctgatggcat amnnmnngaa ggtgcctcca gaagccct

48